(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 141 397**
A2

(12) # EUROPEAN PATENT APPLICATION

(21) Application number: 84113040.4

(51) Int. Cl.⁴: **A 61 J 3/07**

(22) Date of filing: 30.10.84

(30) Priority: 08.11.83 DE 3340262

(43) Date of publication of application:
15.05.85 Bulletin 85/20

(84) Designated Contracting States:
AT BE CH DE FR GB IT LI LU NL SE

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(54) **Divisible hard gelatine capsule and process for the production of them.**

(57) A divisible hard gelatine capsule, particularly for solid or highly-viscous flowable products, consists of two halves which represent opposing semi-circles in cross-section, each with a respective bottom part and a top part which is attached thereto. The sum of the two thicknesses of the capsule halves is somewhat less than the width thereof and the two opposing semi-circular capsule halves are joined approximately in the centre, with respect to the longitudinal axis, so that the divisible capsule can be divided into two parts by twisting them substantially about a transverse axis perpendicular to the opposed planar walls of the capsule halves. The invention further relates to a process for producing the filled divisible hard gelatine capsule.

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BACKGROUND OF INVENTION

Hard gelatine capsules represent an important means for dispensing pharmaceutical products in solid or highly-viscous form, the hard gelatine capsule consistingof a top part and a bottom part, the top part being placed on after the bottom part has been filled and the capsule being sealed i.e. tightly closed in this manner (for example, snap-fit or stor-lock closure). Thus, the hard gelatine capsule also represents a means for dispensing those active materials which are or have to be dispensed in differing doses, partly as such or because smaller doses are dispensed until a normal blood level for the respective treatment is reached or because the active material is dispensed in smaller doses before the patient is completely weaned from the medicament. Children generally require a considerably smaller dose than adults owing to their differing body weight.

Although various doses of the active material can easily be administered in the case of active materials applied by injection of aqueous solutions using syringes of various sizes or by indication of the volume on the syringe - but only by the doctor - and the problem of forming smaller doses can easily be solved by the patient in the case of tablets, for example, by providing grooves to allow the tablets to be broken by pressure, this can only be achieved with hard gelatine capsules by taking in capsules of

differing sizes. However, the mechanical opening, filling and closing operations of the filled hard gelatine capsules are substantially automated, adapted to a small number of standard capsule sizes and the processes for filling and closing the capsules are substantially standardized. The automatic machines used for filling and closing the hard gelatine capsules are extremely bulky and expensive apparatus. The use of hard gelatine capsules of differing sizes would necessitate not only the incorporation of various shaping tools into the apparatus for producing the empty hard gelatine capsules but also the incorporation of at least tools of differing dimensions into the automatic machines for filling and closing the hard gelatine capsules as well as in the packaging machines. As there are no divisible capsules, dimensioning tools of various sizes are required to produce capsules of differing sizes containing varying doses of active material.

The straightforward division of the elongate hard gelatine capsules into two halves, as in the case of tablets, is impossible, as the active materials of the medicament contained therein to be administered are in pulverulent, coarsely-grained, particle-like solid or viscous form, that is in flowable form, and would flow out of the capsule halves if the wall of the capsule was not re-closed after division or was not held closed even during division.

German utility model 81 20 453 proposed a divisible capsule for medicaments which is laterally divisible similar to the manner in which tablets with breaking grooves are divided into two halves. However, this proposal is limited to soft gelatine capsules and cannot be transferred to hard gelatine capsules owing to the fundamentally different materials of the capsule wall and the differing production processes necessitated by this. As is known, (c.f. for example, Kurt H, Bauer, "Die Herstellung von Hart- und Weich- gelatinekapseln", in "Die Kapsel, Grundlage, Technologie und Biopharmazie einer modernen Arzneiform", Wissenschaftl. Verlagsges. mbH, Stuttgart 1983, page 58-81, esp. pages 59 and 60), the soft gelatine capsule can only be filled with the material to be encapsulated during production of the capsule and the filling bulk is limited to liquid products. In contrast, the hard gelatine capsules, with both halves loosely placed on top of each other, are delivered to the drug dispenser and manufacturer, where they are opened, filled and tightly closed by attaching the top part of the capsule onto the bottom part of the capsule in an automatic filling machine. The soft material of the capsule wall alone prevents this method of processing a soft gelatine capsule which has been previously produced being carried out with the automatic filling and closing machines for hard gelatine capsules which frequently operate with ramming devices.

The present invention provides a divisible capsule which the patient can divide very simply and safely into two halves of approximately equal size without loosing the active material of the medicament contained therein. Thus, it is possible to halve the quantity of material in hard gelatine capsules of conventional size and thus halve the dose of active material. Thus, the advantages afforded to the doctor and the patient by a divisible form of dispensing such as tablets or soft gelatine capsules, can also be provided with hard gelatine capsules. In addition, the particularly easy-to-swallow means of dispensing provided by the hard gelatine capsules is rendered even easier to swallow by reducing the capsules into two thinner, relatively more elongate capsules. Moreover, the divisible hard gelatine capsules according to the invention can also be produced using the conventional machines for filling and closing the hard gelatine capsules. The two hard gelatine capsule halves can be joined so as to ensure that the hard gelatine capsule which is filled with a specific dose of the particular medicament cannot be re-opened, a measure which is desired or even necessary for medicaments and in view of the guarantees given by the manufacturers of medicaments and for which purpose particular shapes of capsules, such as the Coni-Snap-Supro capsule have

have been developed by Capsugel for non-divisible hard gelatine capsules.

The divisible hard gelatine capsule according to the invention is characterised in that it consists of two halves which represent opposing semi-circles in cross-section, of conventional length and width, each with a respective top and bottom part, and a top part which is attachable thereto, of conventional length and optional conventional design with respect to preliminary and/or main closing, the sum of the two thicknesses of the capsule halves being somewhat smaller than the thickness of the conventional hard gelatine capsules with a circular cross-section (that is somewhat smaller than the width of the divisible hard gelatine capsule according to the invention), and the two opposing semi-circular halves are joined approximately in the centre, with respect to the longitudinal axis, by a thin, but sufficiently strong strip or web of an easily torn material which surrounds the two semi-circular hard gelatine capsule halves, or by a hidge or a plane bond composed of material which can be easily twisted and torn between the two opposing semi-circular hard gelatine capsules, so that the divisible capsule can be divided into the two halves by twisting them substantially about the transverse axis perpendicular to the plane opposite walls of the semi-circular

hard gelatine capsule halves. The two hard gelatine capsule halves are preferably joined by a strip or by a web or a plane bond or bridge, the strip or the web or the plane bond or the bridge simultaneously jointing the top and bottom part of the two hard gelatine capsule halves of the separable hard gelatine capsule which is finally obtained once it has been filled with the medicament, so that it is not possible to re-open the hard gelatine capsule halves.

The process for the production of the divisible hard gelatine capsules according to the invention is characterised in that unfilled hard gelatine capsules of semi-circular cross-section and of conventional length and width and of a thickness which is somewhat smaller than the width, consisting of a top and bottom part, with the top part placed loosely on the bottom part in conventional manner, are opened in conventional manner, the bottom part is filled with the active material or materials to be encapsulated and the capsule is closed in conventional manner by placing the top part on the bottom part, in which process two of the semi-circular hard gelatine capsules or the top and bottom part thereof are mapped with the plane surfaces thereof opposite each other and are joined together once the semi-circular hard gelatine capsules have been filled and closed, or alternatively two semi-circular hard

gelatine capsules which have been opened, filled and closed in this manner are mapped with the plane surfaces thereof opposite each other and are joined together. The connection is preferably sufficiently wide to join the top and bottom parts of the two opposing hard gelatine capsule halves simultaneously.

As the hard gelatine capsule according to the invention consists of two halves which represent opposing semi-circles in cross-section of conventional length and conventional width with a corresponding top and bottom part having a conventional length ratio to each other, and which are reciprocally semi-circular in cross-section, the sum of the thicknesses of the two capsule halves, including a certain clearance for the bond or the joining web or the joining bridge corresponding to the thickness of conventional hard gelatine capsules of circular cross-section, that is the sum of the thicknesses of the two capsule halves is thus somewhat smaller than the width thereof, it is possible to use semi-circular hard gelatine capsules which have been prefabricated in identical manner and to use the same conventional automatic machines for filling and closing the hard gelatine capsules after modifying the tools to open the semi-circular hard gelatine capsules supplied, that is the halves of the divisible hard gelatine capsules according to the invention, to fill the bottom part of these semi-circular hard gelatine capsules and to close the bottom part with the top part. Existing automatic machines can also be used, after modifying the dimensioning tools, to produce the empty hard gelatine capsule halves. Two immersion pins are used,

instead of the circular immersion pins (poppets or pins), which are of corresponding semi-circular cross-section or which correspond in a side-view to the two elongate halves of the finished divisible hard gelatine capsules according to the invention, for the respective top part and bottom part of the hard gelatine capsules. Likewise, the tools in the automatic filling and closing machines are designed accordingly so that half capsules are supplied in a longitudinal direction to the machine for filling and closing the hard gelatine capsules.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a cross-sectional view of a capsule according to the invention;

Figure 2 is a side view of the capsule of Figure 1;

Figures 3 to 9 illustrate in diagramatical manner how a conventional automatic machine for filling and closing the hard gelatine capsule (e.g. automatic machine GKF 350 by Höfliger and Karg) has to be converted and completed so that it can be used for carrying out the process according to the invention for the production of separable hard gelatine capsules. In particular:

Figure 3 shows a lateral cross-section of an empty capsule container, connected in front of the apparatus, into which the supplied loosely-superposed semi-circular hard gelatine capsules are introduced in unsorted manner.

Figure 4 is a cut-away perspective view on a larger scale of supply paths shown in Figure 3;

Figure 5 shows a segment for receiving capsule halves;

Figure 6 is a lateral cross section through an ejection station;

Figure 7 is a plan view of a bonding station;

Figure 8 is a cross-section of the bonding station of Figure 7; and

Figure 9 is an overall view of the bonding station.

DESCRIPTION OF PREFERRED EMBODIMENT

Figure 3 shows a supply container 1 having an outlet 2 which feeds vertical supply grooves 4 via sloping supply paths 3 (four track in this case, as shown in cross-section in Figure 4). A vibrator 5 is provided at the beginning of the supply path, to allow

conveyance of the capsules. Spring-mounted guide plates 6 are provided at the outlet of the storage container above each oblique supply path 3, which ensure that the hard gelatine capsules are oriented longitudinally with the curvature thereof matching that of the guide grooves and then inevitably place themselves into the grooves 7. The transition to the vertical supply pipes 4 is effected by a rounding of the sloping, that is downwardly-inclined, supply path 3 with the guide grooves . After the capsule halves have been transferred from the grooves into the vertical supply pipes, the pipes describe a 90° rotation with the semi-circular cross-section thereof, more specifically two of the four tubes rotate in opposite directions through90°, that is two to the left and two to the right respectively, so that each two capsule halves are mapped opposite each other with the plane surfaces thereof, when they are transferred into the sorting post.

The hard gelatine capsules lying on their sides (as a plan view) are transferred into the sorting device, carefully pushed forwards horizontally by means of slides adapted to the shape of the capsule, pressed downwards by vertical slides towards the receiving segment 8 shown in Fig. 5, while being oriented such that the bottom part points downwards, as is known from the automatic filling and closing

machines used for known indivisible hard gelatine capsules of circular cross-section. The paths in the sorting device are designed such that the capsules of larger width and/or thickness than the bottom part are held, that is the width and/or depth of the path is smaller than the width and/or thickness of the top part of the capsule, but is greater than the width and thickness of the bottom part of the capsule. The bottom part will thus invariably point downwards owing to the vertical slide, in accordance with the current state of the art in conjunction with the indivisible hard gelatine capsules of circular cross-section.

Supported by a vacuum, the capsules are drawn into the segment and separated, the top part remains in the segment, while the bottom part passes into the guide ring. Fig. 5 shows the arrangement of the bores in the segment and guide ring, the segment 8 resting on the guide ring 9, a section of which is shown. The remainder of the operations for filling the bottom part of the semi-circular hard gelatine capsules and for closing the capsules corresponds to conventionally adopted technology; the bottom part of the capsule is laid free in the guide ring by pushing the upper segment, filling with the active material in pulverulent or other flowable form, the cross-section of the metering tubes generally used for the indivisible circular hard gelatine capsules

having been adapted to the capsule shape described in this case. When introducing the powders, the cross-sections of the ramming devices conventionally used to compact the powders and those of the bores of the powder filling disc are also adapted to the shape of the hard gelatine capsules according to the invention. There then follows the conventional control of the top parts of the capsule, ejection of the faulty capsules, bringing together of the top part and bottom part of the hard gelatine capsule and the closing of the capsules by placing the top part on the bottom part.

An otherwise conventional automatic machine for filling and closing the hard gelatine capsules which has been adapted in this manner is combined with an apparatus for bringing together two respective filled, closed, opposing semi-circular hard gelatine capsules and, for example, a bonding station. The filled, closed halves 10 of the capsules are ejected from the bores of the capsule filling machine by means of ramming devices 11 and with the assistance of compressed air through the channel 12, and the capsule halves are immediately transferred from the bores in the segments into guide tubes 13, this operation corresponding to the ejection of the filled, closed hard gelatine capsules into receiving receptacles, in existing automatic machines for filling and closing indivisible hard gelatine capsules of circular cross-section. This is possible as the capsules are oriented in the apparatus

described herein such that the two respective halves lie with the top and bottom parts thereof adjacent to each other and can thus be joined together. The cross-section of the guide pipes is that of the capsule halves. Figure 6 diagramatically shows a lateral cross-section of an ejection station. In guide tubes 13, the capsules are brought into a horizontal position in the curve of the machine for filling and closing the capsules, the plane sides of each two tubes lying opposite each other. The spacing between each two tubes is simultaneously increased.

Fig. 7 shows a plan view of a cross-section through the bonding station. The guide pipes for conveyance are connected to similar pipes 14 which open with a longitudinal slit 22 (c.f. Fig. 8) on the curved rear side. A continuous rubber entrainment belt 15, equipped with entrainment means 16 at intervals of one capsule length, engages at this point These belts 15 convey the capsule halves 10, and subsequently the capsule halves which have been joined together, to the ejection station which is not shown on this diagram.

An application station 17 for the adhesive (e.g. Methocel in alcoholic solution) is located between the plane sides of the two respective conveying pipes 14, the adhesive being delivered via a membrane 18 on the outside of the plane sides of the top parts of the capsule or of the top and bottom parts.

A groove is provided in the conveying pipes 14 in the region of the adhesive application station until the two capsule halves are brought together.

Once the top parts of the capsule or the top and bottom parts are wetted with adhesive, the two capsule halves are brought together by, for example, a converging of the conveying belts for both capsule halves, and the two capsule halves are then pressed together by means of, for example, the entrainment belt roller 19 and thus bonded. The capsule is then passed through a drying tunnel 20 (not shown) (c.f. Fig. 9), where the adhesive is dried or hardened and is then passed for ejection into the collecting receptacle 21.

Fig. 8 diagramatically shows the cross-section of the bonding station. Storage container 23 and rotating disc 24 are tightly connected to each other, the rotating disc being designed such that the cavity extends to the adhesive-application station 18 projecting from the round form of the disc. The projecting surface which actually applies the adhesive is a web, a membrane or the like. The hydrostatic pressure exerted by the adhesive liquid and the rotation of the disc ensures that the application surface is always saturated with adhesive so that adhesive is always transferred on contacting the surface of the capsule, additionally assisted by the slight pressure exerted by the application surface on the capsule halves passing in

the guide pipe 14. The rotating disc is thus driven by the shaft 25.

Fig. 9 diagramatically shows a total view of the bonding station from the capsule ejector, seen from the automatic filling and closing machines:

Corresponding to the ejection of 2 x 2 opposite semi-circular capsule halves from the filling and closing machine, two bonding stations are arranged parallel to each other. The guide belts 15 and the two bonding apparatus 26 can be controlled by a single drive mechanism. The speed is dependent on the performance of the filling and closing machine, for example about 320 capsule halves/min corresponding to 160 whole separable capsules/min corresponding to 80 separable capsules/min per bonding station 1.5 min are approximately provided as the residence time (throughput time) in the drying tunnel 20 which is from 2 to 3 meters long. The speed and orientation of the conveyor belt and the rotation of the bonding station have to be adjusted such that the plane surface of a capsule top part or top part and bottom part is met and provided with adhesive for each half rotation of the bonding station on each passing guide pipe. It should be ensured when controlling, that the drive mechanism of the bonding station only comes to a halt, each time the machine is shut down, when the application surface is no longer in contact with a capsule.

In order to prevent individual capsule halves which have not been bonded, or which have subsequently broken apart, from being packed, all capsules pass over a vibrating perforated sheet or a screen, (not shown), before packing, so that these are extracted owing to the smaller size of the half capsules, that is the openings are designed such that the whole capsules consisting of two halves which have been tightly bonded together pass on and the capsule halves which have broken open or have not been bonded together fall through the openings.

An alternative to the above bonding of two capsule halves is the gelatine band rolling machine, but it should be noted that bonding is more straightforward and also less expensive.

By designing the bonding station such that the bond is not only placed between the top parts but also at the bottom edge of the top part while covering the adjacent part of the bottom part and is of sufficient thickness and consistency that bonding is also carried out between the bottom parts which are somewhat further away, it is ensured that the divisible hard gelatine capsules according to the invention cannot be opened in the non-divided state thereof, nor after the division thereof.

Claims

1. A divisible hard gelatine capsule, particularly for solid or highly-viscous flowable products, characterised in that it consists of two halves which represent opposing semi-circles in cross-section, of conventional length and width, each with a respective bottom part and a top part which is attached thereto, of conventional length and optional conventional design with respect to preliminary and/or main closing the sum of the two thicknesses of the capsule halves being somewhat less than the width thereof and the two opposing semi-circular capsule halves being joined approximately in the centre, with respect to the longitudinal axis, by a thin, but sufficiently strong, strip or web of an easily torn material which surrounds the two hard gelatine capsule halves or are joined by a bridge or a plane bond between the two opposing semi-circular hard gelatine capsule halves, so that the divisible capsule can be divided into two parts by twisting them substantially about a transverse axis perpendicular to the opposed planar walls of the hard gelatine capsule halves.

2. A divisible hard gelatine capsule according to claim 1, characterised in that the two hard gelatine capsule halves are joined by a strip or by a web or a bridge

or a plane bond, the strip or the web or the bridge or the plane bond simultaneously joining the top and bottom hard gelatine capsule halves of the divisible hard gelatine capsule which are obtained after they have been filled with the solid or highly-viscous flowable product.

3. Process for the production of the divisible hard gelatine capsules according to claim 1, characterised in that unfilled hard gelatine capsules which are loosely superposed on each other, with a top and bottom part, and semi-circular cross-section, and of conventional length and width and of a thickness which is somewhat smaller than the width thereof, are opened in conventional manner, filled with the solid or highly-viscous flowable product to be encapsulated and closed and two of the semi-circular hard gelatine capsules or the top and bottom parts thereof are mapped with the plane surfaces thereof opposite each other and are joined on completion of filling and closing of the semi-circular hard gelatine capsules or two respective filled and closed semi-circular hard gelatine capsules are mapped with the plane surfaces thereof opposite each other and are joined together.

4. Process according to claim 3, characterised in that the connection is applied so wide that it simultaneously joins the top and bottom part of the two opposite hard gelatine capsule halves.

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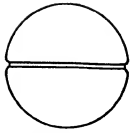

FIG. 1

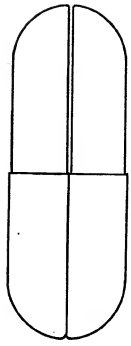

FIG. 2

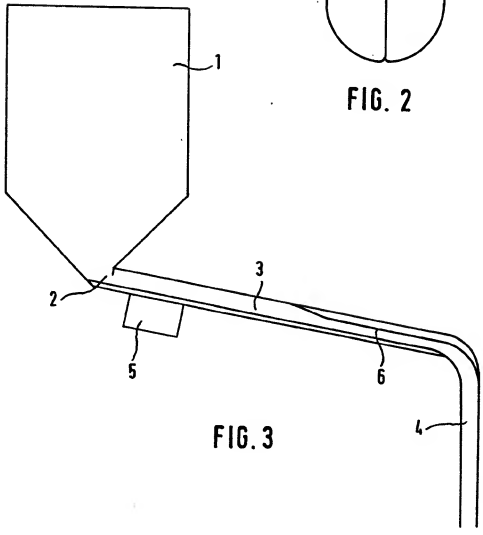

FIG. 3

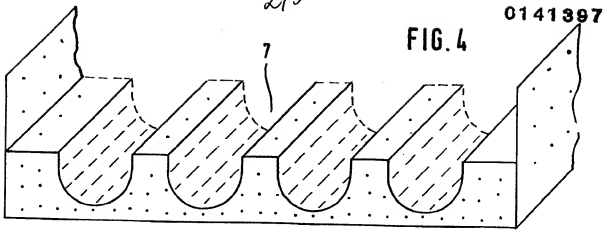

FIG. 4

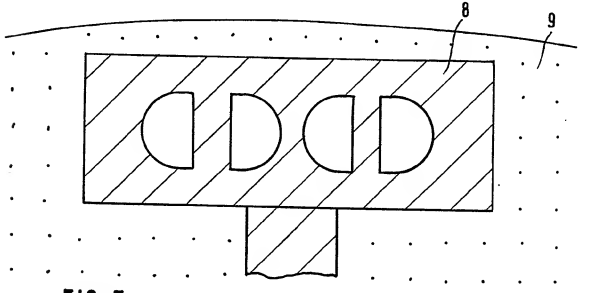

FIG. 5

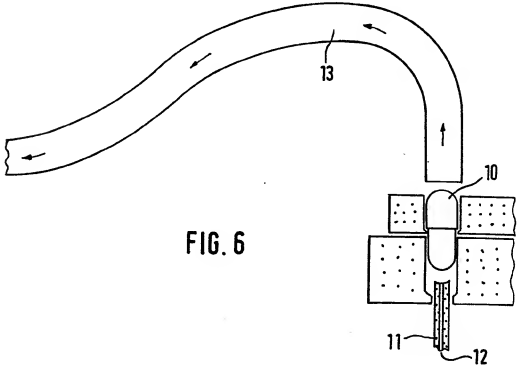

FIG. 6

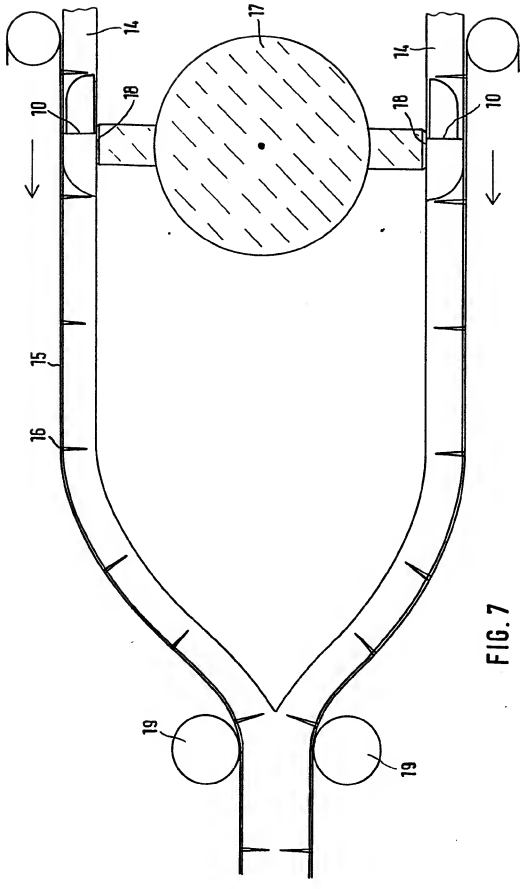

FIG. 7

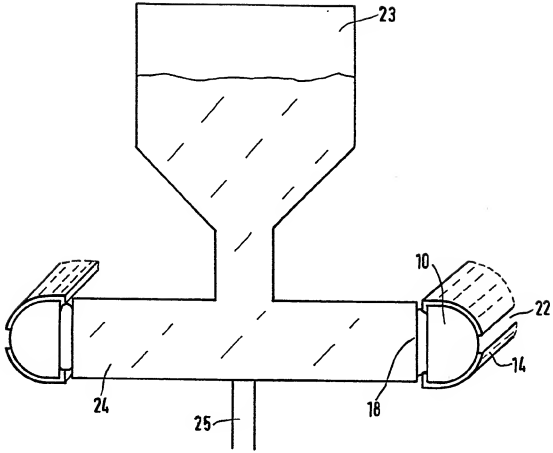

FIG. 8

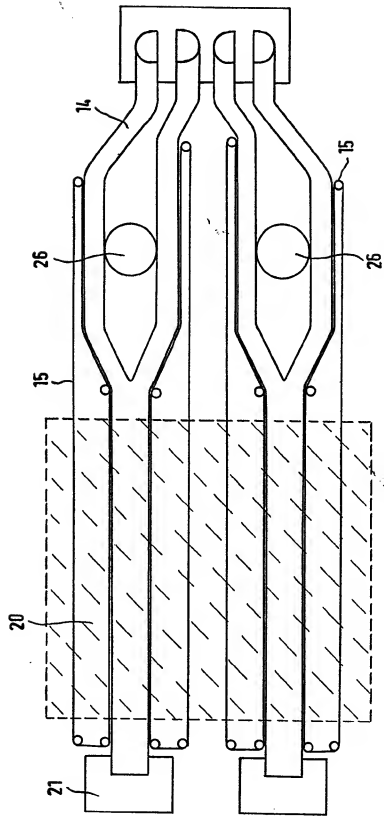

FIG. 9